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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/909,566	07/20/2001	Edgar B. Cahoon	BB1465 US NA	4352

23906 7590 07/15/2003

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EXAMINER

KERR, KATHLEEN M

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 07/15/2003

13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/909,566

Applicant(s)

CAHOON, EDGAR B.

Examiner

Kathleen M Kerr

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 May 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) 7-10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Application Status

1. In response to the previous Office action, a written restriction requirement (Paper No. 11, mailed on April 8, 2003), Applicants filed an election received on May 1, 2003 (Paper No. 12). Claims 1-10 are pending in the instant Office action.

Election

2. Applicant's election without traverse of Group I, Claim 1-6, in Paper No. 12 is acknowledged. Claims 1-10 are pending in the instant application. Claims 7-10 are withdrawn from further consideration as non-elected inventions. Claims 1-6 will be examined herein.

Priority

3. The instant application is granted the benefit of priority for the U.S. Provisional Application No. 60/219,833 filed on July 21, 2000 as requested in the application data sheet. The subject matter of the claims being examined herein is fully disclosed in the provisional document. Thus, for purposes of examination herein, the examined claims have an earliest effective filing date of July 21, 2000.

Information Disclosure Statement

4. The information disclosure statement filed on January 25, 2002 (Paper No. 3) has been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy.

Compliance with the Sequence Rules

5. The sequence listing filed on August 20, 2002 (Paper NO. 10) has been entered. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to **fully** comply with the requirements of 37 C.F.R. § 1.821 through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990).

a) In Figure 1, the first amino acid sequence is not identified by SEQ ID NO. If the noted sequences are in the sequence listing as filed, Applicants must amend the specification to identify the sequences appropriately by SEQ ID NO. If the noted sequences are not in the sequence listing as filed, Applicants must provide (1) a substitute copy of the sequence listing in both computer readable form (CRF) and paper copy, (2) an amendment directing its entry into the specification, (3) a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. § 1.821 (e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d), and (4) any amendment to the specification to identify the sequences appropriately by SEQ ID NO.

Objections to the Specification

6. The specification is objected to because the title is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are drawn (see M.P.E.P. § 606.01). The Examiner suggests the following new title:

---Polynucleotides Encoding a Plant Cytochrome P₄₅₀-like Δ^{12} Epoxygenase---

7. In the specification, the Abstract is objected to for not completely describing the disclosed subject matter (see M.P.E.P. § 608.01(b)). It is noted that in many databases and in foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. The Examiner suggests the inclusion of the full name of the source species, *Euphorbia lagascae*, for completeness.
8. The specification is objected to for lacking continuity data in the first paragraph. The instant application claims the benefit of U.S. Provisional Application No. 60/219,833 filed on July 21, 2000; however, no citation is noted in the first paragraph. Appropriate amendment to the specification is required (see M.P.E.P. § 201.11).
9. The specification is objected to for inappropriate notation of an internet address. On page 9, line 31 and on page 23, line 17, internet addresses are cited in an unacceptable form. See M.P.E.P. § 707.05(e) for the acceptable notation of an internet address.
10. The specification is objected to as being unclear as to its definition of a plant “cytochrome P450 enzyme associated with the synthesis of delta12-epoxy fatty acids” on page 6. This term is called equivalent to a “plant epoxygenase”. Both these terms are defined as “an enzyme that catalyzes insertion of an epoxy group between the 12 and 13 carbon atoms of a fatty acid chain”. This alternate term and this definition suit both the *C. palaestina* epoxygenase (also called a desaturase) and the *E. lagascae* sequence taught in the specification. In contrast to this catalytic definition, the instant specification goes to great lengths to distinguish between the *C. palaestina* epoxygenase enzyme and the *E. lagascae* enzyme taught in the specification (see

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pages 1-2) since the *E. lagascae* enzyme is a cytochrome P₄₅₀-like enzyme and the *C. palaestina* enzyme is not. This understanding in the art is also found in Lee *et al.* (see IDS). In other words, it is the cytochrome P₄₅₀-like nature of the enzyme, not the catalytic activity, that distinguishes the enzyme from previously cloned Δ 12-epoxygenases. Clear recitation of the distinct enzymes is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1 and 3-6 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "cytochrome P450 enzyme associated with the synthesis of delta12-epoxy fatty acids" in Claim 1 is unclear. See discussion of the phrase under Objections to the Specification above on page 6. While it is noted that Applicants may be their own lexicographers, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See M.P.E.P. § 7.34.02 and *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). Particularly the vague phrase "**associated with** the synthesis of delta12-epoxy fatty acids" (emphasis added) is not indicative of the definition provided by the specification. The Examiner suggests inserting the exact function (catalyzing the particular reaction) along with the cytochrome P₄₅₀ requirement in the claim for clarity. For purposes of examination, the following definition will be considered: ---a cytochrome P₄₅₀-like epoxygenase enzyme that

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catalyzes insertion of an epoxy group between the 12 and 13 carbon atoms of a fatty acid chain--
- as reasonably interpreted from the specification.

12. Claim 2 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The nature of a first nucleotide sequence being selected from a first and a second nucleotide sequence is unclear. All references to first and second are extraneous and should be removed for clarity.

13. Claims 3-4 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The antecedent basis of "the isolated polynucleotide of Claim 1" in Claim 3 is unclear since the term "isolated" is not in Claim 1. Clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

14. Claims 1 and 3-6 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the

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application was filed, had possession of the claimed invention. Claim 1 is a polynucleotide claimed solely by function and without any structural limitations.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 1997 U.S. App. LEXIS 18221, at *23, quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus **and** (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

The instant specification describes a single example of the claimed genus, a 1733 base pair polynucleotide encoding a 500 amino acid polypeptide from *Euphorbia lagascae*. The polypeptide is aligned with a pepper polypeptide considered a cytochrome P450 enzyme involved in fungal incompatibility; however, no relation to the epoxygenase function proposed for the disclosed polypeptide is described. Since the disclosed polypeptide is described as the first of its kind (i.e., first structure to have this function), no consensus sequence for cytochrome P450 epoxygenases is described. Additionally, no structure/function relationship is described for the single disclosed species and what would be required for any other species. Therefore, the

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specification does not adequately describe the claimed genus so that one of skill in the art would be able to predict the structure of other members of the claimed genus.

15. Claims 1 and 3-6 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for polynucleotides encoding the disclosed plant epoxygenase, does not reasonably provide enablement for polynucleotides with no structural relatedness and vague functional relatedness to the claimed polynucleotides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The amount of experimentation required of one of skill in the art to use the claimed invention to the full extent of its scope is undue.

The factors to be considered in determining whether undue experimentation is required are summarized in *re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir, 1988). The court in *Wands* states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the

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relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The instant specification provides a single example within the genus of the claimed polynucleotide. No guidance or working examples are present to assist one of skill in the art obtain other polynucleotides within the genus. The art contains few examples of plant epoxygenases and only two examples of cytochrome P450-like plant epoxygenase polypeptides (see Seither *et al.*). There is no indication in the art that any other cytochrome P450-like plant epoxygenases can be found in other plants. In fact, the art is wholly unpredictable considering the isolation of other polynucleotides within the claimed genus. For these reasons, the claims are not enabled to the full extent of their scope.

16. Claim 2 is rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for polynucleotides with at least, for example, 95% sequence identity to a polynucleotide that encodes SEQ ID NO:2, does not reasonably provide enablement for polynucleotides with such low sequence identity, such as the 50% identity claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The amount of experimentation required of one of skill in the art to use the claimed invention to the full extent of its scope is undue.

The factors to be considered in determining whether undue experimentation is required are summarized above.

The specification presents no guidance or working examples of the use of polynucleotides that have such low sequence identity with respect to SEQ ID NO:1. The nature of the invention is such that the DNA encodes a functional protein, a cytochrome P₄₅₀-like epoxxygenase useful in the biosynthetic pathway of vernolic acid and other fatty acids; and with such a great deviation from the known sequence, the predictability of functionality becomes extremely low. Moreover, the instant claims are drawn to DNA sequences that encode a protein which is at least 50% identical to SEQ ID NO:2, and this DNA can automatically be as low as 66% identical to SEQ ID NO:1, the disclosed encoding sequence, due to the degeneracy in the genetic code of the third position of every triplet codon encoding an amino acid of the encoded protein. Therefore, the breadth of the instant claims encompasses at least 50% (due to the claim language) of 66% (due to degeneracy of the genetic code), which is drawn to a nucleotide sequence having as little as 33% identity with the disclosed encoding SEQ ID NO:2. Such enormous breadth and unpredictability renders the instant claims not enabled to the full extent of their scope without undue experimentation.

Claim Rejections - 35 U.S.C. § 101

35 U.S.C. § 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

17. Claim 1 is rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. Claim 1, as written, does not sufficiently distinguish over polynucleotides as they naturally exist because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring

products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 U.S. 303, 206, USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g. by insertion of "isolated" or "purified" as taught by Claim 2 of the specification. See M.P.E.P. § 2105.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 1, 5, and 6 are rejected under 35 U.S.C. § 102(b) as being anticipated by Seither *et al.* (Isolation of cytochrome P-450 genes from *Vernonia galamensis*. Physiology, Biochemistry, and Molecular Biology of Plant Lipids [Proceedings of the International Symposium on Plant Lipids, 12th] (1997) 389-391). The instant claims are drawn to polynucleotides encoding a plant cytochrome P450 epoxxygenase and host cells thereof.

Seither *et al.* teach cDNA encoding a *V. galamensis* cytochrome P₄₅₀ epoxxygenase; no sequence is specifically taught, but the cDNA cloned was sequenced which methods inherently require the cDNA clone in a host cell.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

19. Claims 3-4 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Seither *et al.* in view of Ohlrogge (see IDS). The instant claims are drawn to expression constructs and host cells thereof containing polynucleotides encoding a plant cytochrome P₄₅₀ epoxygenase.

Seither *et al.* teach cDNA encoding a *V. galamensis* cytochrome P₄₅₀ epoxygenase; no sequence is specifically taught, but the cDNA cloned was sequenced which methods inherently require the cDNA clone in a host cell.

Seither *et al.* do not teach expression constructs and/or host cells thereof.

Ohlrogge teaches numerous examples of overexpression of fatty acid metabolism genes for the production of fatty acids useful in industry (see Table II). Specifically, Ohlrogge teaches use of a related desaturase in an expression construct in plant cell.

It would have been obvious to one of skill in the art at the time of the invention to produce expression constructs and host cells thereof of the gene cloned by Seither *et al.* because overexpression of such genes is commonplace in the art as evidenced by Ohlrogge. One would have been motivated to produce such expression constructs and host cells for the purpose of industrially producing vernolic acid, the product of the gene taught by Seither *et al.* since vernolic acid is useful in "paints, plastic formulations, and protective coatings (see Seither *et al.*, page 389). One would have had an expectation of success of being able to produce expression constructs and host cells thereof due to the vast knowledge in the art of recombinant technologies of plants.

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Examiner's Suggestions

20. The following are not rejections, but are the Examiner's suggestions for more suitable claim language to better align the instant claim language with terms of art. While the instant claim language meets the statutory threshold of clarity and precision, a more suitable expression of the claimed subject matter is suggested. Such suggestions are encouraged in M.P.E.P. § 2173.02.

- a) In Claim 4, a ---recombinant--- host cell, as opposed to the claimed "isolated" host cell, is commonly claimed in the art. The word ---recombinant--- should also be added to describe the host cell of Claim 5.

Conclusion

21. Claims 1-6 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (703) 305-1229. The examiner can normally be reached on Monday through Friday, from 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

KMK

July 10, 2003

